

### **Listing of Claims**

1 (Original) An isolated variant platelet derived growth factor receptor alpha (PDGFRA) polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 27, or a fragment thereof comprising at least 10 contiguous amino acids including at least one variant amino acid site as set forth in one or more of positions 560 through 571 or 841 through 848 of SEQ ID NO: 27.

2. (Currently Amended) The isolated variant PDGFRA polypeptide of claim 1, comprising an amino acid sequence as set forth in SEQ ID NO: 4, 6, 8, 10, 12, 21, 23, or 25, or a fragment thereof comprising at least 10 contiguous amino acids including the variant site as set forth in one or more of position 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25, respectively.

3. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 4.

4. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 6.

5. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 8.

6. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 10.

7. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 12.

8. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 21.

9. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 23.

10. (Original) The isolated variant PDGFRA polypeptide of claim 2, comprising the amino acid sequence as set forth in SEQ ID NO: 25.

11. (Original) An isolated nucleic acid molecule encoding the protein according to claim 1.

12. (Original) An isolated nucleic acid molecule encoding the protein according to claim 2.

13. (Original) The isolated nucleic acid molecule of claim 12, comprising a nucleotide sequence as set forth in SEQ ID NO: 3, 5, 7, 9, 11, 20, 22, or 24; or a fragment thereof comprising a variant nucleic acid sequence shown in one or more of position 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

14. (Original) A recombinant nucleic acid molecule comprising a promoter sequence operably linked to nucleic acid molecule according to claim 11.

15. (Original) A cell transformed with a recombinant nucleic acid molecule according to claim 14.

15. – 62. (Canceled)

63. (New) A method of detecting a biological condition associated with an activating PDGFRA mutation in a subject, comprising determining whether the subject has an activating

mutation in PDGFRA, and wherein the activating mutation comprises a variant nucleic acid sequence shown in one or more of positions 2072 through 2107 or 2090 through 2937 of SEQ ID NO: 26.

64. (New) The method of claim 63, wherein the activating mutation comprises a variant nucleic acid sequence shown in one or more of position 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

65. (New) The method of claim 63, which is a method of detecting neoplasia.

66. (New) The method of claim 65, wherein the neoplasia comprises a GIST.

67. (New) The method of claim 63, comprising:  
reacting at least one PDGFRA molecule contained in a clinical sample from the subject with a reagent comprising a PDGFRA-specific binding agent to form a PDGFRA:agent complex.

68. (New) The method of claim 67, wherein the PDGFRA molecule is a PDGFRA encoding nucleic acid or a PDGFRA protein.

69. (New) The method of claim 67, wherein the PDGFRA specific binding agent is a PDGFRA oligonucleotide or a PDGFRA protein specific binding agent.

70. (New) The method of claim 67, wherein the sample comprises a neoplastic cell or is prepared from a neoplastic cell.

71. (New) The method of claim 63 wherein the PDGFRA molecule is a PDGFRA encoding nucleic acid sequence.

72. (New) The method of claim 71, wherein the method comprises HPLC denaturation analysis of a PDGFRA-encoding nucleic acid molecule.

73. (New) The method of claim 71, wherein the agent comprises a labeled nucleotide probe.

74. (New) The method of claim 73, wherein the nucleotide probe has a sequence selected from the group consisting of:

(a) SEQ ID NO: 3, 5, 7, 9, 11, 20, 22, or 24;

(b) fragments of (a) at least 15 nucleotides in length, and including the sequence shown in position(s) 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

75. (New) The method of claim 63, further comprising *in vitro* amplifying a PDGFRA nucleic acid prior to detecting the activating PDGFRA mutation.

76. (New) The method of claim 75, wherein the PDGFRA nucleic acid is *in vitro* amplified using at least one oligonucleotide primer derived from a PDGFRA-protein encoding sequence.

77. (New) The method of claim 76, wherein at least one oligonucleotide primer comprises at least 15 contiguous nucleotides from SEQ ID NO: 3, 5, 7, 9, 11, 20, 22, or 24.

78. (New) The method of claim 76, wherein at least one oligonucleotide primer comprises a sequence as represented by at least 15 contiguous nucleotides shown in position(s) 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

79. (New) The method of claim 68, wherein the PDGFRA molecule is a PDGFRA protein.
80. (New) The method of claim 79, wherein the complexes are detected by western blot assay.
81. (New) The method of claim 79, wherein the complexes are detected by ELISA.
82. (New) The method of claim 79, wherein the PDGFRA protein comprises a sequence selected from the group consisting of SEQ ID NO: 4, 6, 8, 19, 12, 21, 23, and 25.
83. (New) The method of claim 79, wherein the PDGFRA-specific binding agent is a PDGFRA-specific antibody or a functional fragment thereof.
84. (New) The agent of claim 83, wherein the agent is an antibody.
85. (New) The antibody of claim 84, wherein the antibody is a monoclonal antibody.
86. (New) The monoclonal antibody of claim 85, which monoclonal antibody recognizes an epitope of a variant PDGFRA and not an epitope of wildtype PDGFRA.
87. (New) The monoclonal antibody of claim 86, which recognizes an epitope of a variant PDGFRA having an amino acid sequence as shown in SEQ ID NO: 4, 6, 8, 10, 12, 21, 23, or 25.
88. (New) The method of claim 83, wherein the antibody is reactive to an epitope including the amino acid sequence shown in position(s) 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25.

89. (New) A kit for detecting an activating PDGFRA mutation in a subject using the method of claim 31, comprising a PDGFRA protein specific binding agent.

90. (New) The kit of claim 89, wherein the agent is capable of specifically binding to an epitope within a PDGFRA variant protein but not to an epitope of wildtype PDGFRA.

91. (New) The kit of claim 90, wherein the agent is capable of specifically binding to an epitope within:

(a) the amino acid sequence shown in SEQ ID NO: 4, 6, 8, 10, 12, 21, 23, or 25;

or

(b) antigenic fragments of (a) that comprise the sequence shown in position(s) 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25.

92. (New) The kit of claim 89, further comprising a means for detecting binding of the PDGFRA protein binding agent to a PDGFRA polypeptide.

93. (New) The kit of claim 89, wherein the subject is a mammal.

94. (New) The kit of claim 93, wherein the mammal is a human.

95. (New) The kit of claim 89, wherein the PDGFRA protein binding agent is an antibody.

96. (New) A kit for determining whether or not a subject has a biological condition associated with an activating PDGFRA mutation by detecting a mutant PDGFRA sequence in the subject, comprising:

a container comprising at least one oligonucleotide specific for a PDGFRA mutation sequence; and

instructions for using the kit, the instructions indicating steps for:

performing a method to detect the presence of mutant PDGFRA nucleic acid in the sample; and

analyzing data generated by the method,

wherein the instructions indicate that presence of the mutant nucleic acid in the sample indicates that the individual has or is predisposed to the biological condition.

97. (New) The kit of claim 96, wherein the method to detect the presence of mutant PDGFRA nucleic acid in the sample comprises HPLC denaturation of a PDGFRA-encoding nucleic acid molecule.

98. (New) The kit of claim 96, further comprising a container that comprises a detectable oligonucleotide.

99. (New) The kit of claim 96, wherein the biological condition associated with the activating PDGFRA mutation is neoplasia.

100. (New) The kit of claim 96, wherein the at least one oligonucleotide specific for a PDGFRA mutation sequence comprises the sequence shown in position(s) 2919 of SEQ ID NO: 3, 2917 and 2918 of SEQ ID NO: 5, 2927 and 2928 of SEQ ID NO: 7, 2075 to 2080 of SEQ ID NO: 9, 2089 to 2093 of SEQ ID NO: 11, 2076 of SEQ ID NO: 20, 2017 and 2072 of SEQ ID NO: 22, or 2916 to 2919 of SEQ ID NO: 24.

101. (New) The kit of claim 99, wherein the neoplasia comprises a GIST.

102. (New) A method of screening for a compound useful in influencing PDGFRA-mediated neoplasia in a mammal, comprising determining if a test compound binds to or interacts with the polypeptide or fragment according to claim 1, and selecting a compound that so binds.

103. (New) The method of claim 1027, wherein binding of the compound inhibits a PDGFRA protein biological activity.

104. (New) The method of claim 102, wherein the test compound is applied to a test cell.

105. (New) A compound selected by the method of claim 102.

106. (New) The compound of claim 105, for use as a therapeutic agent.

107. (New) A composition comprising at least one antigenic fragment of the protein of claim 1, where the antigenic fragment includes the variant sequence as shown at position(s) 842 of SEQ ID NO: 4, 841 and 842 of SEQ ID NO: 6, 845 and 846 of SEQ ID NO: 8, 561 and 562 of SEQ ID NO: 10, 565 and 566 of SEQ ID NO: 12, 561 of SEQ ID NO: 21, 559 and 560 of SEQ ID NO: 23, or 841 and 842 of SEQ ID NO: 25.